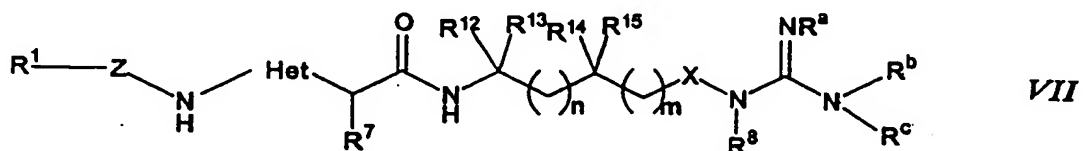


Heteroaryl Aminoguanidines and Alkoxyguanidines and Their Use as Protease Inhibitors

Abstract

Aminoguanidine and alkoxyguanidine compounds are described, including compounds of the Formula VII:



5 wherein X is O or NR⁹ and Het, R¹, R⁷, R⁸, R¹²-R¹⁵, R^a, R^b, R^c, Z, and n are set forth in the specification, as well as hydrates, solvates or pharmaceutically acceptable salts thereof, that inhibit proteolytic enzymes such as thrombin. Also described are methods for preparing such compounds. The compounds of the invention are potent inhibitors of proteases, especially trypsin-like serine proteases, such as chymotrypsin, trypsin, thrombin, plasmin and factor Xa.

10 Certain of the compounds exhibit antithrombotic activity via direct, selective inhibition of thrombin. The invention includes a composition for inhibiting loss of blood platelets, inhibiting formation of blood platelet aggregates, inhibiting formation of fibrin, inhibiting thrombus formation, and inhibiting embolus formation in a mammal, comprising a compound of the invention in a pharmaceutically acceptable carrier. Other uses of compounds of the

15 invention are as anticoagulants either embedded in or physically linked to materials used in the manufacture of devices used in blood collection, blood circulation, and blood storage, such as catheters, blood dialysis machines, blood collection syringes and tubes, blood lines and stents. Additionally, the compounds can be detectably labeled and employed for *in vivo* imaging of thrombi.